Case Report

Acute Pustular Dermatosis, Following Topical Treatment With Pimecrolimus, in a Child Affected With Atopic and Contact Hand Dermatitis

Dimitri Poddighe, MD,[1] Valeria Brazzelli, MD,[2] Amelia Licari, MD,[3] and Gian Luigi Marseglia, MD[3]

[1]Department of Pediatrics, Azienda Ospedaliera di Melegnano, Milan, Italy; [2]Department of Dermatology, Fondazione IRCCS Policlinico San Matteo; [3]Department of Pediatrics, Fondazione IRCCS Policlinico San Matteo–Universita' degli Studi, Pavia, Italy

Atopic dermatitis is considered an important risk factor for chronic hand dermatitis, which can be seen in children too. Pimecrolimus cream 1% is approved to treat atopic dermatitis in children aged 2 years or older. In adults, this drug has been used for some clinical indications other than atopic dermatitis, such as chronic hand dermatitis. Here, we describe an adverse drug reaction in a 2-year-old child affected with atopic dermatitis, who was treated with topical pimecrolimus in order to ameliorate her concomitant hand dermatitis. The use of topical pimecrolimus led to a previously undescribed hand pustular dermatosis, being consistent with a form of pustular leukocytoclastic vasculitis, which required the permanent discontinuation of topical pimecrolimus.

INDEX TERMS: adverse drug effect, atopic dermatitis, Elidel cream, pediatric, pimecrolimus, pustular dermatitis

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INTRODUCTION

Chronic hand dermatitis (CHD) is a relapsing skin disease characterized by pruritic eczematous lesions being variably associated with aspects of lichenification and/or hyperkeratosis. Chronic hand dermatitis is often associated with irritant/occupational factors, but it can arise in the clinical setting of atopic dermatitis (AD). In fact, AD is considered an important risk factor for CHD.[1,2]

Allergic contact CHD can be seen in children. The impairment of the skin barrier of patients affected with AD can facilitate the allergic sensitization to several substances. As a consequence, allergic contact dermatitis should be considered in children experiencing recalcitrant AD and/or CHD, which represent an indication to perform patch tests for environmental allergens or chemicals.[3,4]

Topical calcineurin inhibitors (TCIs), including pimecrolimus cream 1% (Elidel cream, Meda Pharma SPA, Milan, Italy), have been approved for the treatment of AD in children.[5] Currently, in adults TCIs have been experimented to treat other inflammatory skin diseases, including contact dermatitis and, particularly, CHD.[6] Here, we report a hand pustular dermatosis following the use of topical pimecrolimus in a pediatric patient affected with AD and CHD.

CASE REPORT

An Italian 2-year-old female child of white ethnicity had been followed because of moderate AD since she was younger than 1 year. In addition to diffuse skin dryness/itching and the typical involvement of neck/face, elbows, knees, and wrists, this patient showed severe eczema with papules and lichenification at both hands, especially on the palmar surfaces. The AD improved significantly through a careful medical management, which included topical corticosteroids and antibiotic therapy for a couple of weeks, followed by the administration of montelukast (4 mg/day), and, of course, optimal skin care and use of emollients as a maintenance therapy.

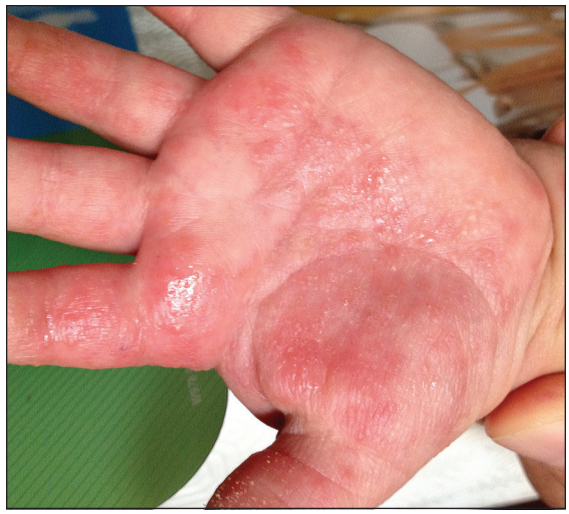

Figure 1. Chronic hand dermatitis before topical treatment with Elidel cream.

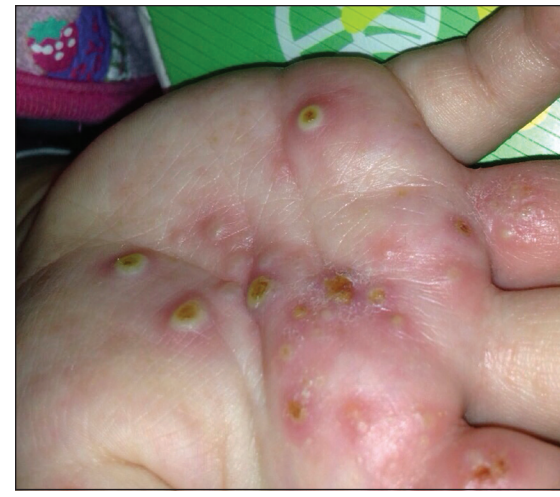

Figure 2. Hand pustular dermatitis following topical treatment with Elidel cream.

Another important aspect of the clinical management was the avoidance of ascertained allergic trigger factors and of potential irritants. Indeed, the child was patch tested, showing sensitization to several agents, namely potassium dichromate, phenylpropil-*p*-phenylenediamine, and dermatophagoides mixture. Therefore, environmental dust mite decontamination was recommended and this was done by the parents.

Almost complete remission of AD was achieved through such a clinical management. However, CHD ameliorated only slightly (Figure 1) and, especially on the palmar surface, significant itching and eczema have persisted. Therefore, topical treatment with pimecrolimus 1% cream was started and administered twice a day. Unfortunately, around 5 to 7 days after the beginning of this treatment, the parents again brought the child to our attention because of an unexpected worsening of the hand disease. The patient developed a pustular dermatosis limited to the palms, where pimecrolimus cream was used (Figure 2). The blood count and the inflammatory parameters (including C-reactive protein and erythrocyte sedimentation rate) were found to be negative, and there was no fever.

This acute hand pustulosis was investigated through several microbiologic examinations of the material obtained from the pustules, but no bacterial, viral (e.g., herpesviruses), or fungal infection was identified. Actually, a non-resistant strain of *Staphylococcus aureus* was isolated from a cutaneous swab performed on the skin surface, but it was thought to be a colonization. Based on this finding, amoxicillin-clavulanate was started anyway. Despite this approach, there was no improvement during the first few days; thus, pimecrolimus 1% cream was stopped.

Then, a special skin care was recommended too, which consisted of a hand compress with water solution containing potassium permanganate (1:10,000) and bandages with a galenical containing vioformio (1 g), vaseline (50 g), olive oil (15 g), and zinc oxyde (10 g). After these recommendations and after stopping topical pimecrolimus, such a pustular exanthem resolved completely in a couple of weeks. Patch tests to pimecrolimus and vehicle substances contained in Elidel cream were suggested to the parents, but they refused to consent because of the concern about further skin adverse reactions in their child.

DISCUSSION

We reported a previously undescribed adverse skin reaction following the initiation of topical treatment with pimecrolimus 1% cream, which was used to ameliorate CHD in a child affected with AD. Pimecrolimus 1% cream is considered an effective steroid-sparing topical treatment for mild to moderate AD in children older than 2 years.[7] A further advantage of topical pimecrolimus is its safe use on sensitive skin areas, where topical steroids could cause skin alteration (e.g., cutaneous atrophia, striae, telangectasias, hypopigmentation) or its absorption could be en-

hanced.[8] Conversely, the use of topical pimecrolimus in children has been somewhat limited by concerns raised about the theoretical risk of skin malignancy. However, the evaluation of the risk of malignancy in more than 7000 children of the Pediatric Eczema Elective Registry, providing a follow-up period greater than 25,000 person-years, concluded that pimecrolimus 1% cream is very unlikely to cause malignancy.[9]

Among new emerging indications of TCIs in adults there is CHD, which is often a very concerning skin disease, as irritant or allergic trigger factors are very difficult to eliminate.[6] A randomized study by Belsito et al[10] in patients affected with CHD of various etiologies showed a clinical improvement with pimecrolimus 1% cream. Actually, a greater double-blind randomized trial, which included 652 adult patients with mild to moderate CHD, did not confirm a significant difference between the treated group and patients receiving only the vehicle; however, the relief of itching, which is an important end-point in this clinical setting, was significantly higher in treated patients.[11]

In our patient, despite a more general improvement of AD through an appropriate skin care, the use of montelukast and the avoidance of environmental irritant and allergic factors, CHD and its related itching remained an important clinical complaint, and therefore topical treatment with pimecrolimus was prescribed. Unfortunately, this treatment had to be stopped as soon as 8 to 10 days after its initiation because of the onset of an acute pustular dermatosis localized to the hand surfaces where topical pimecrolimus cream had been placed.

Studies assessing the safety of TCIs rarely reported significant local adverse reactions other than burning, feeling of warmth, mild pain, or stinging.[12] Pimecrolimus-related dermatitis has been seen in 3% of treated adults, and another study reported a rate of local reactions (including contact dermatitis) being lower than 5% in children.[13] However, in the medical literature we found only one case of allergic contact dermatitis (without pustules) that occurred after use of Elidel cream, because of sensitization to oleyl-alcohol in a 20-year-old patient who had been affected since childhood with CHD in the setting of AD.[14]

Our case represents the first report of a local adverse reaction that occurred after the initiation of a treatment with topical pimecrolimus 1% cream, leading to such a pustular dermatosis. Although *Staphylococcus aureus* colonization has been found on palmar surfaces, the purulent/neutrophilic material contained in the pustules was actually sterile. Indeed, the antibiotic treatment alone was not beneficial, and improvement of the overlapped pustular skin disease was observed only after the topical pimecrolimus was discontinued.

Therefore, an infectious etiology does not appear to be a consistent cause of such a pustular dermatosis. Although it is unusual in the first decade of life, these palmar skin lesions could have suggested pustular psoriasis,[15] but the dermatologic picture showed no chronic course and did show a strong temporal link to the use of topical pimecrolimus. Actually, such a clinical picture might resemble pustular leukocytoclastic vasculitis, which can be associated with an underlying bacterial infection/colonization, in the presence of other concomitant trigger factors impairing or altering the immune system.[16] Interestingly, there are descriptions of palmoplantar pustular dermatosis following systemic immunosuppressive therapy, and, particularly, a case of leukocytoclastic vasculitis has been reported in a patient who underwent transplantation, after the initiation of therapy with systemic calcineurin inhibitors, namely sirolimus.[16,17]

Challenging our case report by using an adverse drug reaction probability scale proposed by Naranjo et al,[18] we could label this medical event as being a probable adverse reaction to topical pimecrolimus, given a probability score of 6 points. Indeed, such a skin reaction appeared only after the use of topical pimecrolimus and was strictly localized to the areas where it was applied. Moreover, this pustular dermatosis ameliorated only when the topical pimecrolimus was discontinued, regardless of the antibiotic therapy that was initially prescribed, and no alternative explanations to this clinical event are evident. Given the rarity of skin reactions during the use of topical pimecrolimus, some potential predisposing factors that should be considered include bacterial colonization, drug use on palmar surfaces, patient's young age, and concomitant therapy with montelukast. In conclusion, it is likely that such a hand pustular leukocytoclastic dermatitis was triggered by the treatment with topical pimecrolimus, considering the consistent

temporal association, the location of skin lesions, and the anlysis of this event through an appropriate probability scale for adverse drug reactions.

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Abbreviations AD, atopic dermatitis; CHD, chronic hand dermatitis; TCIs, topical calcineurin inhibitors

Correspondence Dimitri Poddighe, MD, Department of Pediatrics, Azienda Ospedaliera di Melegnano, Milan, Italy, email: dimimedpv@yahoo.it

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